ABSTRACT OF THE DISCLOSURE

Methods and devices are provided for determining the presence and/or concentration of at least one analyte in a sample of low transmissivity. In the subject methods, a forward beam and a backward beam are produced by or introduced into an interferometer from at least one infrared radiation source. The forward beam is passed into the sample and then collected to produce a sample beam while the backward beam is passed into a reference and then collected to provide a reference beam. The sample and reference beams are recombined either optically into a null beam which is detected at a single detector or electronically nulled after detection on two separate detectors. The presence, and often amount, of at least one analyte in the sample is then derived from the detected null beam. Also provided are devices for practicing the above methods. The subject methods and devices are suitable for use in a variety of different applications, including the detection of the presence, and amount, of one or more blood analytes in a physiological sample, such as blood, tissue or derivatives thereof.